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(54) Apparatus for monitoring neuromuscular transmission and method of monitoring neuromuscular blockage.

(57) To determine the degree of neuromuscular blockage, the apparatus of the invention electrically, supramaximally stimulates the motor nerve of a patient by stimulus means, applies the resulting electromyogram (EMG) produced by the muscle associated with that motor nerve and integrates the amplified EMG with respect to time. The integrated, amplified EMG is then displayed. In a preferred embodiment of the invention means are also provided for displaying the integrated, amplified EMG, taken after a muscle relaxant has been administered to the patient, as a ratio of a control EMG taken with the apparatus before the administration of the drug.
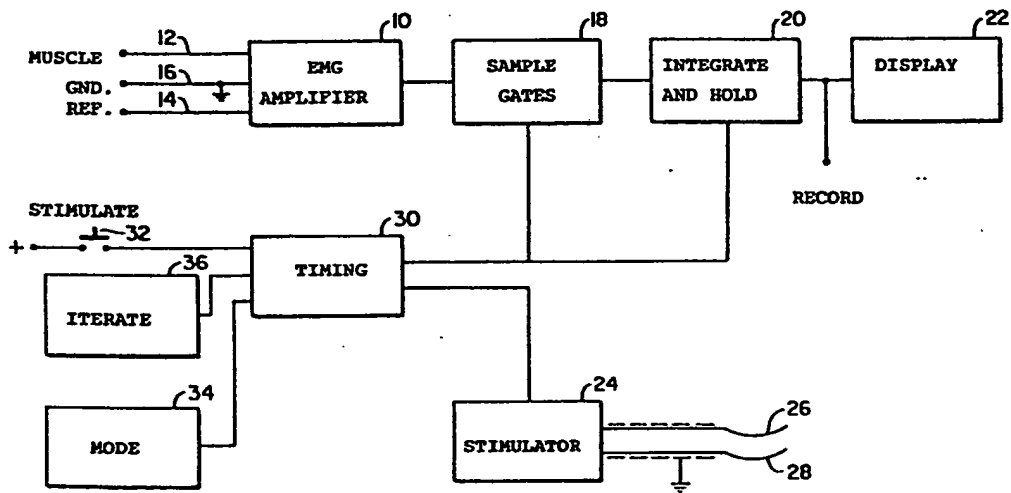
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MUSCLE 12
GND. 16
REP. 14

EMG
AMPLIFIER 10

SAMPLE
GATES 18

INTEGRATE
AND HOLD 20

DISPLAY 22

RECORD

STIMULATE

32

TIMING 30

ITERATE 36

STIMULATOR 24

26

28

MODE 34

FIG._1.

Description

Apparatus for Monitoring Neuromuscular Transmission and Method of Monitoring Neuromuscular Blockage

Technical Field

5   This invention relates to devices and methods for determining the degree of neuromuscular blockage produced by the use of muscle relaxant drugs to a patient. More specifically the present invention relates to apparatus for monitoring neuromuscular transmission.

10   ### Background Art

During many surgical operations it is important to relax the patient's muscles by administering drugs such as curare, and the like. If the does of the relaxant drug is given in the correct amount, the effects of the

15   drug will wear off after surgery and the patient will regain his or her ability to breathe naturally, with little after-effects. If, however, an overdose is given, an extended paralysis and other after-effects may occur which are highly undesirable. What is needed is a way

20   to continually measure the percentage of the completeness of the neuromuscular block produced by the muscle relaxant drug both during and after the operation. Clinical experience has shown that optimal muscle relaxation is obtained when a block is about 95% complete (5% of control).

25   A more complete block is usually not needed and may lead to prolonged recovery or difficulty in reversing the blockage.

After surgery antagonist drugs are administered to the patient to reverse the effect of the muscle relaxants.

30   In some cases, however, the blocking drugs originally administered to the patient may outlast the antagonists, resulting in a recurrence of weakness in the recovery room. It is therefore important to be able to monitor

the degree of neuromuscular blockage during the administra-
tion of the antagonist drugs. The way in which the anta-
gonist drugs work is to help the patient's body utilize
chemicals produced within the nerve cells to reestablish

5 control. These chemicals are subject to depletion as
control is regained, producing an effect known as fading.
In such a condition, the initial amount of control in
response to a single stimulus may be satisfactory but this
control fades with repeated stimuli following immediately

10 after the first stimulus. To check for fading it is
necessary to measure the amount of neuromuscular blockage
using tetanus stimulation.

Among the prior art methods and devices for monitoring
neuromuscular blockage, the most widely used is a portable

15 battery-operated stimulator without a meter. The anesthe-
siologist watches the movement of a muscle such as a
finger, thumb or facial muscle after a twitch or tetanic
stimulus. For research purposes, and occasionally for
clinical monitoring, some prior art devices have employed

20 strain gauges or force transducers which are taped to a
digit to permit recording of the strength of the contrac-
tion. See, for example, U.S. Patent Nos. 3,898,983 and
3,565,080 (Ide).

This technique requires a separate amplifier and

25 recorder. Furthermore, such devices are highly inaccurate
and subject to spurious signals as the digit to which the
strain gauge has been taped is moved during surgery,
thus providing unreliable information. Another problem
with measuring the twitch of a digit or other muscle as an

30 indication of neuromuscular blockage is that the two are
not linearly related. In some cases the muscular twitch
will disappear before the EMG is fully blocked.

Another proposal is to record the EMG response from
the patient. The EMG signal impulse is too fast for

35 conventional direct writing pen recorders and the like, so
that users have employed oscilloscopes and photographic

recording. A recent device has been reported in which
an EMG amplifier digitizes the response in a memory, such
as a magnetic tape or magnetic disc. This digitized
memorized signal is then played back a few seconds later
5 at a much slower rate into a pen recorder or the like.
Aside from the time delay in obtaining the response,
this device also requires elaborate and expensive electronic
equipment.

Summary of the Invention
10 The above and other disadvantages of prior art
neuromuscular transmission monitoring apparatus are over-
come by the present invention which comprises means for
electrically, supramaximally stimulating a motor nerve,
means connected to the stimulus means for receiving and
15 amplifying the resulting electromyogram (EMG) produced
by the muscle associated with the motor nerve, means
connected to the EMG amplifier means for integrating
the amplified EMG with respect to time, and means connected
to the integrator means for displaying the integrated,
20 amplified EMG.

In the preferred embodiment of the invention, the
display means further comprises simple and direct means
for displaying the ratios of EMG's obtained from a patient
after the administration of the muscle relaxant drug to
25 a reference standard (i.e., control) EMG which is taken
with the same monitoring apparatus, but before the admini-
stration of the muscle relaxand drug. In this embodiment
the readout from the apparatus is expressed as a percentage
of the control response.

30 The stimulus means include mode control means for
selectively causing the production of either a single
pulse (twitch), a train of pulses (tetanus), or a train of
a predetermined number of pulses at regular intervals.
Further included are iterating means to automatically
35 cause the stimulus means to repeatedly generate stimulus

pulses at predetermined intervals. The stimulus pulses
which are repated can be either the twitch, tetanus or
train of predetermined number of pulses.

The amplifier means includes a gate which is triggered
5   by the stimulus pulse for gating the amplifier means on a
predetermined time after the stimulus pulse and for
thereafter holding the amplifier means on for predetermined
period of time to allow the integration of the resulting
EMG. In the preferred embodiment the amplifier means
10 includes rectifier means for passing only negative polarity
EMGs of the appropriate frequency. This feature, combined
with the gating feature, avoids artifacts from the stimula-
tor and other noise sources.

In one embodiment of the invention, the display means
15 includes a digital circuit for automatically comparing the
resulting EMG to the control EMG and digitally displaying
the output as a percentage of the control EMG.

In contrast to some prior art devices which simply
measure the EMG by mechanical transducer means, for example,
20 the response signal measured by the present invention is
instantaneously processed by integration of the EMG nega-
tive output, thereby giving area rather than peak height.
Some drugs and conditions cause a broadening of the
response due to delayed conduction in some neural or motor
25 units, and under such circumstances, the area under the
response is a better index of total transmission than is
peak height. The present invention avoids the need to
mechanically fix a force transducer to a digit, and to
immobilize the hand and guard it from disturbance by
30 surgeons and nurses standing at the operating table. It
also avoids the use of such fragile and expensive trans-
ducers.

Furthermore, the present invention permits improved
monitoring in clinical anesthetic practice, by giving a
35 quantitative, continuous indication of the degree of
neuromuscular blockage, thus permitting more careful

determination of the dosage of neuromusuclar blocking
drugs and their antagonists. With present visual monitor-
ing of the muscular response, it may be difficult to
determine whether a weak response is present or not.

5   Since the device of the present invention is portable
and self-contained, it may be left attached to the patient
after surgery, during transport to the recovery area, and
during recovery, to monitor the return of neuromuscular
transmission. As mentioned above, this is an important

10 feature since in some cases, the blocking drugs may out-
last the antagonists, resulting in a recurrence of weakness
in the recovery room.

     Since the stimulator and EMG amplifier are combined,
the synchronization of the amplifier gate is built in. In

15 all units now in use, a synchronization pulse must be
externally connected from the stimulator to the amplifier
for accuracy. The voltage and current characteristics of
such sync signals are not standardized among the various
units.

20   It is therefore an object of the present invention
to provide a portable neuromuscular blockage monitor.

     It is another object of the present invention to
provide a neuromuscular blockage monitor in which the
stimulator and response meter are combined into a single

25 unit.

     It is yet another object of the invention to provide
a neuromuscular blockage monitor which requires no
connection to electrical power lines.

     It is a further object of the invention to provide

30 a neuromuscular blockage monitor in which the neuromus-
cular response during blockage is measured and displayed
directly as a percentage of the control response.

     It is yet a further object of the present invention
to provide a neuromuscular blockage monitor which is

35 responsive to the area of EMG response rather than to
peak height.

It is yet another object of the invention to provide
a neuromuscular blockage monitor having easily selected
modes of operation including twitch, train of four, or
tetanus stimulation pulses.

5   It is still another object of the invention to provide
a neuromuscular blockage monitor which repeatedly and
automatically stimulates and monitors at predetermined
time intervals.

Brief Description of the Drawings

10   The foregoing and other objectives, features and
advantages of the invention will be more readily understood
upon consideration of the following detailed description
of certain preferred embodiments of the invention, taken
in conjunction with the accompanying drawings, wherein:

15   FIGURE 1 is a block, schematic diagram of the
neuromuscular block monitor according to the invention;

FIGURE 2 is a detailed schematic diagram of the
neuromuscular block monitor depicted in FIG. 1; and

FIGURE 3 is a schematic diagram of a portion of a
20 modified embodiment of the invention.

Best Mode for Carrying Out Invention

Referring now more particularly to FIG. 1, a
differential amplifier 10 receives the electromyogram
signal from two electrodes 12 and 14, which are self-
25 adhesive skin surface, EKG-type electrodes. Electrode 12
is placed over a particular muscle and the reference
electrode 14 is placed nearby on the patient's skin, but
not on that muscle. The ground electrode, of course,
is attached to the patient at some other location. Ampli-
30 fied EMG signals from the amplifier 10 are supplied to a
sample gate 18. The purpose of the sample gate is to allow
the amplification of only negative EMG signals received
1.5 microseconds after the stimulus is applied and for a
duration of 8 milliseconds. The frequency response of the
35 amplifier 10 is constant $\pm$ 3db from 10Hz to above 2KHz.

The amplified signals passed by gate 18 are supplied to an integrator 20 which integrates and stores or holds the area under EMG response curve. The integrated signal from the integrator 20 is supplied to a display 22.

5   A stimulator 24 is connected to the patient by a pair of skin surface electrodes 26 and 28. The active stimulus electrode 26 is affixed over the motor nerve of the patient which controls the muscle over which the electrode 12 is positioned. The stimulus return electrode 28 is attached

10 to the patient nearby the electrode 26.

The stimulator is controlled by a timing circuit 30. The timing circuit is activated initially either by a push-botton stimulate switch 32 or automatically at timed inter-vals after an iterate switch 36 is operated. A mode selec-

15 tor switch 34 is also connected to the timing circuit to determine what type of stimulus pulse is to be supplied by the stimulator 24. As will be explained in greater detail hereinafter, the mode switch 34 allows at least four types of stimulus pulses to be applied to the patient. In

20 the first position a single twitch pulse is supplied to the patient. In the second position a train of four such twitch pulses are supplied at half second intervals. The third and fourth positions of the mode switch apply tetanus pulses for differing periods of time to the patient. The

25 tetanus train consists of repeating stimuli every 20 milliseconds (50Hz). In the third position of the mode switch, the tetanus train lasts two seconds and in the fourth position the tetanus train lasts for 0.1 seconds.

As mentioned above, the iterate switch 36 selectively

30 causes the timing circuit 30 to repeat whatever mode was selected at predetermined timed intervals.

In operation, when the mode selector switch 34 is positioned in the twitch mode, a 0.15 millisecond square wave pulse is supplied from the stimulator to the patient

35 through the electrodes 26 and 28 when the stimulate switch 32 is depressed. The timing circuit 30 and the sample and

hold gate 18 do not begin to pass the output from the EMG
amplifier 10 through to the integrator 20 until 1.5
milliseconds after the stimulus. This ensures that what-
ever signal is received by the electrodes 12 and 14 and
5 is amplified by the amplifier 10 will be the true EMG in
response to the stimulus and not noise or artifacts from
the stimulator. The EMG amplifier 10 amplifies the EMG
signal, and the negative portion of that signal is passed
by the gate 18 to the integrator 20 for the following 8
10 milliseconds. At the end of the 8 millisecond period,
the timing circuit turns off the sample gate 18 and the
integrated EMG output from the integrator 20 is held and
displayed on the display 22.

Referring now more particularly to FIG. 2, the system
15 will be described in greater detail. The electrode 12 is
coupled through a capacitor 36 and a resistor 38 to the
plus input of a differential amplifier 40. Similarly the
reference electrode 14 is coupled through a capacitor 42
and a resistor 44 to the plus input of a second differen-
20 tial amplifier 46. The ground electrode 16 is connected
to the circuit ground and also to the mid-point of a pair
of resistors 48 which are connected in series between the
resistors 38 and 44. A voltage divider network 50,
connected between the output of the amplifier 40, the
25 output of the amplifier 46 and the circuit ground, subtracts
the output of the amplifier 46 from the output of the
amplifier 40 so that only the difference of the two outputs
is fed through a capacitor 52 connected to the output of
the amplifier 40. The amplifiers 40 and 46 are thus in an
30 instrumentation configuration.

The difference signal supplied through the capacitor
52 passes through a resistor 54 to the source or drain
electrode of a field effect transistor 56, to the plus
input of a comparator 58, and to the source or drain
35 electrode of a second field effect transistor 60. The other
of the source or drain electrodes of the FET 60 is connected

to the circuit ground as is the negative input to the
comparator 58. The other of the source and drain electrodes
of the FET 56 is connected through a potentiometer 62 to
the negative input of an integrating, differential ampli-
5   fier 64 whose other input is connected to the circuit
ground.

The output of the comparator 58 is connected to the
anode of the diode 66 whose cathode is connected through
a resistor 68 to the negative bias controlled gate elec-
10   trode of the FET 56.

The gate electrode of the FET 56 is also connected
to the cathode of a diode 70 whose anode is connected
through a resistor 72 to the positively controlled gate
electrode of the FET 60 and the output of a comparator
15   74. The positive input to the comparator 74 is connected
to one side of a capacitor 76, whose other side is grounded,
and through a resistor 78 to the anode of a diode 80. A
positive bias is provided to the input of the comparator
74 by means of a resistor 82 connected between the plus
20   bias source of the circuit and the anode of the diode 80.
A capacitor 84 is also connected between the anode of the
diode 80 and the circuit ground.

In operation, unless a negative pulse is applied to
the cathode of the diode 80, the output of the comparator
25   74 will be positive and, passing through the diode 70,
will cause the FET 56 to be non-conductive and the FET 60
to be conductive, so that no signal will pass through the
potentiometer 62 to the integrating amplifier 64. When
a negative level is applied to the cathode of the diode 80,
30   it will serve to discharge the capacitor 84 and then the
capacitor 76 over a time period determined by the product
of the resistance of the resistor 78 and the capacitance
of the capacitor 76. When the capacitor 76 is no longer
positive, the comparator 74 will produce a negative bias
35   and thus the FET 60 will become open circuited and the FET
56 will become conductive depending on the output of the
comparator 58.

If the signal being supplied to the FET 56 through
the resistor 54 is positive, the comparator 58 provides a
positive bias to the FET 56, thereby causing it to become
non-conductive. Negative going signals, on the other hand,
5 drive the comparator 58 negative permitting the transistor
56 to be conductive (when comparator 74 output is also
negative) and pass through the FET 56 and the resistor 62
to be integrated by the integrating amplifier 64 in a
manner to be described in greater detail hereinafter.
10 Thus only negative going signals are integrated in the
applicants' device and only those signals appearing during
the time period required to recharge the capacitor 76
through the resistors 78 and 82 (approximately 8 millise-
conds).

15 The output of the integrating amplifier 64 is supplied
to a recorder terminal 86. Terminal 86 is connected through
a resistor 88 to an intermediate terminal 90, which in
turn, is connected through a second resistor 92 to the
circuit ground. The purpose of the terminal 90 is to pro-
20 vide a low voltage or scaled version of the signal appearing
at the terminal 86.

The output of the amplifier 64 is also connected through
a resistor 93, a switch 94 and a resistor 96, in series,
to one lead of a meter 98 which constitutes the display 22.
25 The other lead of the meter 98 is connected through a
second switch 100 to the circuit ground.

The integrating return path from the output of the
amplifier 64 is through a capacitor 102 connected to the
negative input of the amplifier 64 and to the moving con-
30 tact of the potentiometer 62. An FET 104 is connected to
selectively shunt the capacitor 102 when the FET 104
becomes conductive. A switch 106 is connected in parallel
with the resistor 93 to provide for alternate voltage
scale readings on the meter 98.

In operation, the amplified EMG signal from the differential amplifier 10 is integrated by the amplifier 64 at a rate determined by the product of the capacitor 102 and the resistance of the resistor 62. Thus, the
5 setting of the contact arm of the potentiometer 62 determines the rate of integration.

In the preferred embodiment of the invention the method under which this operation is carried out begins by providing a stimulus to the patient before the administration
10 of the muscle relaxant. At this time the contact arm has been moved fully to the right so that the slowest rate of integration is utilized. The meter is then read for that control EMG. The meter scale will run from 0 to 100. Assuming that the meter reads some number less than 100,
15 for example 30, then the contact arm of the potentiometer 62 is accordingly adjusted to present 30% of the full resistance of the potentiometer 62. With suitable scaling the contact arm can simply be dialed to a number 30 on a linear indicating dial (not shown). It should be noted
20 that the winding of the potentiometer 62 is linear so that a 30% of full scale position will present a corresponding 30% of full resistance. The next reading of a controlled stimulus signal will be full scale on the meter. Subsequent readings for EMGs produced after the administration
25 of a muscle relaxant will produce meter readings which are some amount less than full scale and therefore can be directly read as a percentage of the controlled stimulation response. For example, an EMG reading taken after the administraiton of a muscle relaxant which showed a
30 meter reading of 40 would indicate that the muscle relaxant block is 60% complete (40% of control).

The switches 94 and 100 are single pole double throw switches and can be moved to an alternate position from that shown in FIG. 2 to connect the meter 98 to the batter-
35 ies to check their voltage level.

The gate of the FET 104 is connected through a
resistor 110 to the collector of an NPN transistor 116
which is part of the stimulator circuit 24. The emitter
of the transistor 116 is connected to the negative bias
5   terminal of the power supply 108. The base of the trans-
istor 116 is connected to an input trigger line 118 of
the stimulator circuit 24. It will be appreciated that
when the transistor 116 is made conductive by the applica-
tion of a current pulse to the base of 116 the collector
10 electrode will become negative, thereby applying a negative
pulse to the gate electrode of the FET 104 and causing it
to become conductive. As will be explained in greater
detail hereinafter, this occurs whenever the stimulator
circuit 24 is triggered with the effect that the integra-
15 tor circuit 20 is simultaneously reset to zero when the
FET 104 becomes conductive.

The details of the stimulator circuit 24 will now be
described. The trigger line 118 is connected through a
capacitor 120 in series with a resistor 122 to the collec-
20 tor of a PNP transistor 124. The collector of the transis-
tor 124 is connected through the primary winding of a
transformer 126 to a negative terminal of the power supply
108. The emitter of the transistor 124 is connected to a
positive terminal of power supply 108. A capacitor 128
25 is connected between the positive and negative terminals
of the power supply 108. A diode 130 is connected at its
anode to the negative terminal of the power supply 108 and
at its cathode to the collector of the transistor 124. The
base of the transistor 124 is connected through a resistor
30 131 to the collector of the transistor 116.

In operation, when a current is applied to the base of
transistor 116, the transistor 116 becomes conductive and
turns on the transistor 124, thereby providing a current
pulse to the primary of the transformer 126 and a corres-
35 ponding stimulus pulse to the electrode probes 26 and 28.
A voltage limiting circuit 132 is connected between the
collector and base of the transistor 124, through resistor

168 and capacitor 170, and the negative terminal of the power supply 108. The purpose of the circuit 132 is to regulate the pulse height of the stimulus pulse applied to the electrodes 26 and 28 independent of the load on

5 the battery operated power su-ply 108. When the pulse voltage on the collector of 126 reaches the specified level set by zinc diode 172, transistor 132 conducts, and sends current through capacitor 170 to prevent further increase in base current in transistor 124. Capacitor

10 120 and resistor 122 provide increased (decreased) base current drive to transistor 116 on the rising (falling) edge of the signal at transistor 124, thus providing faster, more stable turn on (off) transistor 116, thereby providing a stable pulse to the patient.

15 The trigger pulse to the line 118 is supplied by the timing circuit 30. The timing circuit 30 comprises a comparator 134 whose positive input is connected through a capacitor 136 in series with the stimulator switch 32 to a positive terminal of the power supply 108. The

20 output of the comparator 134 is connected through a resistor 138 in series with a capacitor 140 to the positive input of the comparator 134. The output of the comparator 134 is also connected to the positive terminal of the power supply 108 by means of a suitable biasing resistor 142.

25 The positive input terminal of the comparator 134 is also connected to a negative terminal of the power supply 108 through a resistor 144.

When the stimulate switch 32 is closed, a positive pulse is applied to the input of the comparator 134 which

30 amplifies the pulse and provides a positive output back to its own input through the resistor 138 and the capacitor 140. This positive output continues for about two seconds until the capacitor 140 is discharged by the resistor 144. The output of the comparator 134 will then flip suddenly

35 to the negative power supply (due to the bias through resistor 144). Thus the time constant produced by the product of the capacitor 140 and the resistor 144 deter-mines the duration of the positive output pulse from the

comparator 134 when the stimulus switch 32 is closed.

The output of the comparator 134 is also connected
through a capacitor 146 to the anode of a diode 148. The
cathode of the diode 148 is connected through a resistor
5 150 to the trigger line 118. The output of the comparator
134 is also connected to the moving contact of the iterate
switch 36 and one of the moving contacts of the mode switch
34. The fixed contact terminals of this portion of the
mode switch 34 are all connected to the anode of the diode
10 148 with the exception of one unconnected contact at the
train of four setting of the switch 34.

The iterate switch 36, when in the off position,
shunts a diode 152 whose anode is connected to the output
of the comparator 134 and whose catho-e is connected through
15 a resistor 154 to the positive input of a second comparator
156. When the iterate switch 36 is in the on setting, it
is unconnected, for purposes of the operation of the
circuit.

The output of the comparator 156 is connected to the
20 anode of a diode 158 whose cathode is connected to the
cathode of diode 148. The negative input to the comparator
156 is connected to the circuit ground. The positive input
to the comparator 156 is connected to the anode of the
diode 112 and also through a capacitor 160 to the circuit
25 ground. The output of the comparator 156 is further con-
nected to the anode of a diode 162 whose cathode is connect-
ed to the moving contact of the second portion of the
swtich 34. The fixed contact terminals of the second
portion of the switch 34 have the following connections.
30 At the twitch setting the contact is connected to the anode
of the diode 114. At the train of four setting the contact
is connected through a resistor 164 to the anode of the
diode 114. At the two-second tetanus pulse setting, the
contact is unconnected and at the 0.1 second tetanus
35 setting, the contact is connected through a resistor 166
to a negative terminal of the power supply 108.

The operation of the timing circuit 30 and the
stimulator 24 depend on the settings of the three switches
32, 36 and 34. The resulting EMGs in all cases will be
detected, amplified, rectified, integrated and displayed
5   in the manner heretofore described. Assuming that the
iterate switch 36 is turned off and that the mode switch
34 is set in the twitch setting, when the stimulus switch
32 is pressed the comparator 134 will provide an enabling
positive pulse through the switch 34, the diode 148 and
10 the resistor 150 to the trigger line 118. When the stimu-
lator 24 provides the stimulus pulse to the probes 26 and
28, as outlined above, a negative pulse will be sent back
from the collector of the transistor 116, through the diode
114 and the second portion of the switch 34 to the positive
15 input of the comparator 134. The effect of the negative
pulse is to discharge the capacitor 140 and reset the
comparator 134 to a negative output. Thus a single
twitch stimulus pulse has been provided.
    With the mode switch 34 set at the train of four
20 position, as it appears in FIG. 2, closing of the stimulus
switch 32 causes the comparator 134 to again provide an
enabling pulse to the trigger line 118 through the capaci-
tor 146, the diode 148 and the resistor 150. This enabling
pulse is also provided to the capacitor 160 to charge it
25 from its initial negative potential derived from the
previous negative output of the comparator 134. The capa-
citor 160 charges to a positive potential through the
switch 36 and the resistor 154 after about one-half second
to produce a positive output from the comparator 156 which
30 is supplied to the trigger line 118. This causes the
stimulator to again trigger and again produce a negative
reset pulse through the diode 112 to discharge the
capacitor 160.
    This process will be repeated as long as the output
35 of the comparator 134 remains positive, which is for
approximately two seconds. Provided the correct resistance
and capacitance values have been chosen, four such stimulus

pulses are generated. In order to ensure that only four
such pulses are provided the negative pulse occurring on
the last of the four pulses, and which passes through the
diode 114 and the resistor 164, serves to discharge the
5   capacitor 140 of any remaining residual charge near the
end of the two second interval. This also ensures that
no significant recharging of the capacitor 160 takes
place after the fourth such stimulus pulse. If this were
not done, then the next cycling using the comparator 156
10   for iteration or train of four mode would not be accurate.
        With the mode switch set at either the two-second
tetanus or 0.1 second tetanus, the output of the compara-
tor 134 is again provided to the trigger line through
the first portion of the mode switch 34, the diode 148
15   and the resistor 150. As long as a positive bias is
provided to the trigger line 118, the stimulator will
oscillate at 50Hz with an on time of 0.15 milliseconds.
The oscillation rate is a product of the resistance of
the resistor 150 and the capacitance of the capacitor 120
20   whereas the on time of 0.15 milliseconds is determined by
the product of the capacitance of the capacitor 120 and
the resistance of the resistor 122. The duration of this
tetanus train is determined by the product of the capaci-
tance of the capacitor 140 and the resistance of the
25   resistor 144 (in the two second mode) or the resistance
of the resistor 166 (in the 0.1 second mode).
        The purpose of the iteration switch 36 is to cause
any selected mode to be repeated at approximately 10
second intervals. When the switch 36 is set to "on,"
30   i.e., it is opened, then the quiescent, negative polarity
output of the comparator 134 is not applied to the
capacitor 160 because of the diode 152. The capacitor
160 will slowly charge to a positive polarity through a
resistor 155 connected to a positive terminal of the
35   power supply 108. Once the charge becomes positive the
comparator 156 will trigger the stimulator 24 as well as

supply a positive input to the comparator 134. At that point the timing circuit will behave just as though the stimulate switch 34 will be executed. Ultimately the capacitor 160 is charged negatively by the negative pulse

5 supplied from the stimulator circuit 24 through the diode 160. The capacitor 160 will then begin to recharge through the resistor 155. This process will be repeated at timed intervals, e.g., every 10 seconds, as determined by the product of the resistance of the resistor 155 and

10 the capacitance of the capacitor 160.

Referring now more particularly to FIG. 3, an alternative embodiment of the present invention is illustrated in which the output display is in digital form. This embodiment may be implemented while omitting certain com-

15 ponents from the embodiment depicted in FIG. 2 and replacing those components with circuitry shown in FIG. 3. The labelled components from FIG. 2 which are omitted are components 18, 58, 60, 62, 66, 68, 70, 72 and 110, as well as the entire meter circuit. In addition to the power and

20 ground connections between the two sections of the circuit there are two other connections, the collector of transistor 116 is connected, as shown in FIG. 3, and the output of comparator 74 is connected, as shown on FIG. 3, in addition to any other connections which may be present

25 on FIG. 2. The output of the instrumentation amplifier 10 is taken through capacitor 52 to the signal input of a high speed integrating means 174. This means may typically comprise an input resistor, a feedback capacitor and an operational amplifier. In addition there is a clamping

30 diode and a field effect transistor. The output of the integrator 174 is fed into the inverting input of a comparator 176. The non-inverting input of the comparator 176 is driven by the output voltage of a type D to A converter 178. The function of the D to A converter will

35 be explained later. The output of the comparator 176 with appropriate level shifting feeds to the reset transistor within the integrator 174 and in operation, the sequence is as follows.

When a negative input voltage appears at the input of
the integrator 174, the output integrator is caused to
ramp positive. When the voltage exceeds the output
voltage of the D to A converter 178, the output of the
5 comparator 176 changes state going low, that is negative,
and causing the reset switch on the integrator 174 to
reset it to zero. As soon as the integrator 174 reaches
zero, or approximately thereabouts, the comparator 176
then changes state and releases the drive to the reset
10 transistor within the integrator 174 allowing the integra-
tor to again begin integrating the signal. This cycle
is repeated and generates a pulse train whose frequency
is proportional to the input voltage divided by the D to
A converter output voltage. The transfer equation is
15 given as follows:

$$F_{out}^{(t)} = \frac{V_{in}^{(t)}}{V_{DAC}} \times \frac{1}{RC} \; H_z \quad (\text{for } \underline{\text{negative}} \; \underline{V_{in}} \; \underline{\text{only}}; \; F_{out}=0Hz \text{ for } \overline{V_{in}} \; \overline{0})$$

$$V_{DAC} = -\frac{\text{"Digital In" x } V_{ref}}{1023} \; \text{Volts} \quad (\text{"Digital In"} = \text{Count})$$

$$Count = \int_{o}^{8 \, m'sec \, (t)} F_{out} \, dt \quad (\text{dimensionless})$$

The integrator, comparator and D to A converter output
20 voltage form what is known in the trade as a voltage to
frequency converter 180 and may be implemented in one of
several different ways. This pulse train from the compara-
tor 176 is also fed to a counter section, which in the
figure as shown consists of two different counters 182 and
25 184. It is possible by appropriate manipulation of digital
circuitry to allow using only one counter. This pulse
train from the comparator 176 goes into the clock inputs
respectively, of a 10 bit counter 184 and a 3 digit BCD
counter 182. BCD stands for binary code decimal. The
30 output of the 10 bit counter 184 feeds by way of gating
logic 186 to the digital inputs of the D to A converter

178. The 10 bit counter 184 is used to collect and store the control pulse, i.e., the control EMG signal as defined earlier.

The D to A converter 178 then converts this digital
5 representation of the control signal into a voltage representation mention-d before as the output voltage of the D to A converter. The digital gating logic 186 is provided to allow presetting the D to A converter 178 to a decimal value of 100 that is a binary value of
10 0001100100. This value of 100 is chosen so that when the control signal is stored it will be referenced to a 100 signal and therefore when the control value is fed into the 10 bit bit counter 184 and then back into the D to A converter 178 at the end of the collection of the
15 control signal, all subsequent storage signals will be referenced to the control signal divided by 100 thus giving a readout in percent. The switch 188 shown connected to the gate 186 is a normally open, momentary switch and may be defined as the control preset switch.
20 It is held down for and during a collection of a control signal from the patient.

When the switch is closed it biases an AND and OR gates at the D to A converter 178 to provide a decimal of 100. In addition it provides an enabling signal for
25 the 10 bit counter 184 which is used in two ways. First this enabling signal is anded with the buffered and level shifted signal (by buffer and level shifter 195) from transistor 116 collector mentioned before, which feeds through an AND gate 190 to the reset port of the 10 bit
30 counter 184. Thus, when one is storing a control signal this .15 millisecond pulse from 116 collector will reset the control register to zero before the counter is to be enabled to then store the control signal. The switch connection also controls another AND gate 192. The other
35 input of the AND gate 192 feeds from the comparator 74 output through a converter buffer level shifter 194 to the enabling input of the 10 bit counter 184.

Returning to the 3 digit BCD counter 182, this is the
display accumulator and storage counter. It also is fed by
the enabling reset lines from the comparator 74 output and
transistor 116 collector, respectively, which perform the

5   same function as they did on the 10 bit counter only these
are not gated by the switch 188. Thus, with each stimulus
and respective EMG response this counter 182 is reset and
then a little bit later is allowed to accumulate counts
from the voltage to frequency converter 180. The outputs

10 from this counter are fed into standard decoding logic 196
and converted to a format capable of driving a liquid
crystal display 198. The resistor shown on the pole of the
switch 188 is simply used to assure that the digital logic
lines are not floating when that switch is open and may be

15 any convenient value from 1K to 1 megohm depending on the
size circumstances. Note: All of the digital logic is
presumed to be implemented in Cmos technology and is
readily available in a commercial market in the United
States in many different prepackaged forms. As mentioned

20 before, it is not necessary to use two counters. An
example of how to use only one counter would be to use the
three digit BCD counter feeding the outputs of the decoding
logic display and also feeding the outputs to three four
bit batches which then feed the D to A converter through

25 the gating logic. A similar, but not exactly the same,
method for resetting enabling the latch is used. The
advantage of using the latches is it simplifies by reducing
the number of gates required to preset the D to A converter
to 100. However, it has its own requirement for its own

30 additional control circuitry in the form of 1 or 2 gates.
If the latch version is used, the D to A converter must be
a three digit BCD input D to A converter; if the 10 bit
counter version is used then the D to A converter is more
simply a ten bit binary D to A converter. The D to A

35 converter may be of any standard type which has a voltage
output or may be a current output type with an appended
operational amplifier to convert the current into a voltage.

It may use an extra low voltage reference or have its own
internal voltage reference which will be scaled for the
appropriate value for this particular circuit.

In either of these alternative embodiments the func-
5 tion of resistor 62 is changed. This resistor no longer
needs to be a variable resistor. It may be a fixed resis-
tor of appropriate value to set the time constant for the
RC circuit of the integrator to appropriate value.

The sequence of events in collecting the control and
10 then subsequently collecting and displaying a sample
will now be briefly summarized. The operator of the unit
selects the level of stimulus desired and sets the selec-
tor switch 34 to single twitch. The operator then presses
the stimulus button 32 causing the stimulator section 24
15 of the circuit to apply its signal voltage to the nerve
causing the muscle to put out its EMG waveform which is
amplified by the amplifier as described earlier. The
amplified EMG is fed through capacitor 52 and is then
present during the 8 or so milliseconds duration of that
20 response at the input to the high speed integrator 180.
When the input to the high speed integrator is positive,
the integrator will attempt to drive this output downwards,
however, the clamping diode prevents it from going very
far negative. When the input signal is negative, the inte-
25 grator quickly recovers and begins integrating in a positive
direction and then goes through the sequence of events des-
cribed earlier, driving the comparator 176 output state
low and being reset, and then again integrating upwards
and subsequently doing the same thing with the comparator
30 176 creating the pulse train mentioned before. The switch
188 being closed has preset a value of 100 into the D to
A converter 178 which is translated into the appropriate
output voltage by the D to A converter. Thus the control
EMG signal is referenced to the voltage equivalent of the
35 digital 100. Meanwhile, the two counters 182 and 184 have
been reset by the pulse from 116 collector and have been

enabled by the 74 output changing state. The pulse train
is sent into both the 10 digit counter 184 and the 3 digit
BCD counter 182 and is accumulated there during the appro-
ximately 8 milliseconds of the sampling period. Those

5 counters are then disabled. The value in the three digit
BCD counter 182 is identical to the value of the 10 bit
counter 184 only in the encoded format of the BCD as
opposed to the binary encoding. The three digit BCD num-
ber is then fed directly onto the display 198, allowing

10 the operator to observe to so-called raw value of the con-
trol signal which should be somewhere between 50 and 999.
Thus, there is a wide range of response variations which
are allowed for this control signal, namely of practically
a 20 to 1 dynamic range for inputs.

15   The 10 bit counter 184 now contains a binary represen-
tation of the control EMG signal in integrated form. The
operator now opens the preset switch 188. This whole pro-
cess takes less than a second. Opening the switch 188
prevents the 10 bit counter 184 from being enabled or reset

20 by subsequent signals and allows the 10 bit value stored
in that counter to be fed directly through the the D to A
converter.

        The output of the D to A converter then instantly
assumes the voltage equivalent of whatever the digital

25 integral of the EMG signal happens to be. As mentioned,
this can be somewhere between 50 and 999. Note: The
counter has a capability of storing numbers up to 1023
but the output counter can only display up to 999.

        The output voltage of the D to A converter 178 now

30 corresponds to the integrated value of the control EMG
and will be used as the reference voltage for the voltage
to frequency converter 180 for all subsequent signal
collections. To collect and store a sample EMG the
operator merely presses stimulus switch 32 or sets the

35 iterate switch. The amplifier 10, the high speed inte-
grator 174 and the comparator 176 work in identical
fashion as mentioned before except that the comparator
reference voltage is now proportional to the integrated

control voltage. The 10 bit counter 184 is not affected by the two reset and enabling control signals and maintains its count. The three digit BCD counter is reset and enabled appropriately and at the end of the 8 milli-

5 second window contains the new EMG signal as a fraction of the control signal.

The signal then is immediately displayed on the LCD display 198 and the operator can then observe that and note whatever physiological indications this may give.

10 The terms and expressions which have been employed here are used as terms of description and not of limitation, and there is no intention, in the use of such terms and expressions of excluding equivalents of the features shown and described, or portions thereof, it being recog-

15 nized that various modifications are possible within the scope of the invention claimed.

Claims

1. Apparatus for monitoring the neuromuscular trans-
mission of a motor nerve and the muscle associated with the
nerve in a patient, the apparatus characterized by
         a stimulator for generating an electrical signal
5 and for applying it to the motor nerve to supramaximally
stimulate it,
         an amplifier and detector circuit which is connected
to the stimulator and including a pair of sensing electrodes
attached to the patient, for sensing the electromyogram (EMG)
10 produced by the associated muscle as a result of the stimu-
lating electrical signal and for amplifying the EMG,
         an electronic integrator circuit connected to the
amplifier and detector for receiving the amplified EMG and
for integrating it with respect to time,
15   control standard means connected to the integrator
for storing a representation of a first integrated EMG,
         a comparator connected to the integrator for
generating an output signal which is representative of the
ratio of a select, integrated EMG and the first, integrated
20 EMG, and
         means for displaying the output signal of the
comparator.

2. Apparatus as recited in claim 1 wherein the control
standard means produce a reference signal representative of
25 the integrated and stored first EMG, and wherein the compa-
rator includes means for resetting the integrator to a pre-
determined initial value whenever the integrated EMG output
of the integrator exceeds the reference signal.

3. Apparatus as recited in claim 1 or 2 wherein the
30 comparator generates an output signal which is representative
of the integrated, amplified EMG's obtained from a patient
after the administration of a muscle relaxant drug as a ratio
of a reference standard EMG taken with the monitoring appa-

ratus before the administration of a muscle relaxant drug.

4. Apparatus as recited in claim 1 wherein the ampli-
fier and detector circuit are further characterized by an
electronic gate which is triggered by the stimulus pulse
5 for gating the amplifier and detector circuit on a pre-
determined time after the stimulus pulse and for thereafter
holding the amplifier and detector circuit on for a pre-
determined time.

5. Apparatus as recited in claim 1 wherein the stimu-
10 lator is characterized by a mode control circuit for select-
ively producing either a single pulse, a rapid series of
pulses, or a predetermined number of pulses at regular
intervals.

6. Apparatus as recited in claims 1 or 5 wherein the
15 stumulator is further characterized by an iterating circuit
to automatically cause the stimulator to repeatedly generate
stimulus pulses at predetermined intervals.

7. Apparatus as recited in claim 1 wherein the ampli-
fier and detector circuit is further characterized by a
20 rectifier for passing only negative polarity EMG's.

8. Apparatus as recited in claims 1 or 7 wherein the
stimulator is further characterized by a pair of skin elec-
trodes, one placed over the motor nerve and one placed nearby
and further wherein the stimulator applies a square wave
25 stimulus pulse to the electrode over the nerve relative to
the other electrode of the pair.

9. A method of monitoring neuromuscular blockage in a
patient characterized by the steps of
        electrically, supramaximally stimulating a motor
30 nerve of a patient before the administration of a muscle
relaxant drug,

detecting and amplifying the resulting electro-
myogram (EMG) produced by the muscle associated with the
stimulated motor nerve,

integrating and holding the amplified EMG with
5 respect to time to obtain an integrated control EMG,

repeating the stimulating, amplifying, inte-
grating and holding steps after the administration of a
muscle relaxant drug to the patient to obtain an integrated
EMG at less than full control, and
10 displaying the ratio of the integrated, non-full
control EMG to the control EMG.

10. The method as recited in claim 9 characterized in
that the second set of stimulating, amplifying, and inte-
grating steps are repeated after the administration of a
15 muscle relaxant drug followed by the administration of an
antagonist drug.

11. The method as recited in claims 9 or 10 wherein
in performing the second integrating step the rate of
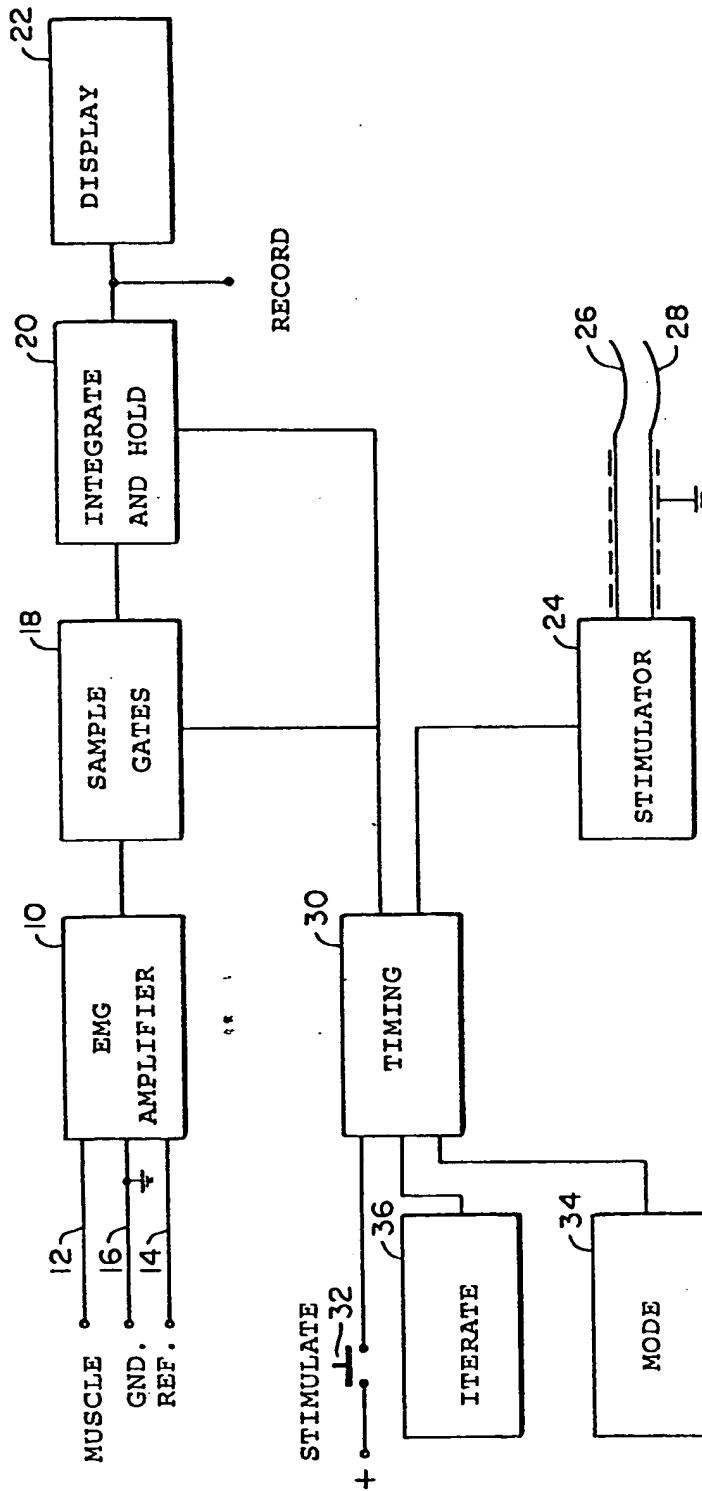integration is a function of the integrated control EMG.

FIG.__I.

FIG._2.

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FIG._3.